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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
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ART UNIT	PAPER NUMBER
1649	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/664,423	ROULEAU ET AL.	
	Examiner	Art Unit	
	Daniel Kolker	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14,17,20 and 23-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14,17,20,24 and 25* is/are rejected.

7)☒ Claim(s) *23* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *See Continuation Sheet*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :4/27/07, 5/30/07, 6/22/07, 6/29/07.

DETAILED ACTION

1. The remarks and amendments filed 29 June 2007 have been entered. Claims 1 – 13, 15 – 16, 18 – 19, 21 – 22, and 26 – 29 are canceled. Claims 14, 17, 20, and 23 – 25 are pending and under examination.

Continued Examination Under 37 CFR 1.114

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 29 June 2007 has been entered.

Withdrawn Objections and Rejections

3. The following rejections and objections set forth in the previous office action are withdrawn:

A. The rejection under 35 USC 102(b) as anticipated Mandel (WO 96/14077) is withdrawn in light of the amendments. Independent claim 14 now requires at least 95% identity to SEQ ID NO: 1 or to the full-length complement thereof, whereas the sequence from Mandel does not have this degree of identity.

B. The rejection under 35 USC 102(b) as anticipated by Noda is withdrawn in light of the amendments. Independent claim 14 now requires at least 95% identity to SEQ ID NO: 1 or to the full-length complement thereof, whereas the sequence from Noda does not have this degree of identity.

C. The rejection under 35 USC 103(a) as unpatentable over Noda is view of Wang is withdrawn in light of the amendments. As Noda does not anticipate the independent claim, it cannot be used as a primary reference over the rejected dependent claims.

D. The rejection under 35 USC 112, second paragraph is withdrawn in light of the amendments which clarify the scope of claims 14 and 24 and which cancel claim 15.

E. The rejection under 35 USC 102(b) over Stratagene catalog is withdrawn in light of the amendments. Independent claim 14 now requires at least 95% identity to SEQ ID NO: 1 or to the full-length complement thereof, whereas Stratagene product is short fragments of nucleic acid sequences and does not have the required degree of identity.

F. The rejection under 35 USC 102(e) over Furness (US 6,673,549) is withdrawn in light of the amendments. Independent claim 14 now requires at least 95% identity to SEQ ID NO:1 or to the full-length complement thereof, whereas Furness product does not have the required degree of identity over the full length.

Maintained Rejections and Objections

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14, 17, 20, and 24 – 25 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleic acids at least 95% identical to SEQ ID NO:1 which encode sodium channels, does not reasonably provide enablement for nucleic acids at least 95% identical to SEQ ID NO:1 as broadly claimed, and does not reasonably provide enablement for the full scope of nucleic acids "wherein the presence of said nucleic acid in a sample of a subject indicated that the subject has an increased risk of idiopathic generalized epilepsy" as recited in claim 24. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

This rejection stands for the reasons previously made of record. SEQ ID NO:1 encodes a human sodium channel. Parts (a) and (b) of claim 14 are enabled over their entire scope. However, part (c) of claim 14 is not enabled over its full scope. The prior art of record recognized that sodium channels are useful proteins, and that they are crucial in propagation of action potentials. The specification discloses many possible uses of sodium channels, and notes that there are several activities that are common to sodium channels (see for example paragraph spanning pp. 19 – 20). It is within the skill of the artisan to determine how to make and how to use variants of SEQ ID NO:1 which both retain 95% sequence identity and which encode sodium channels. However, claim 14 encompasses variants of SEQ ID NO:1 with any function at all or with no function whatsoever. There is no requirement that any particular structural elements be retained, there is no requirement that the nucleic acid variants have any particular function on their own, and there is no requirement that the nucleic acid variants

encode functional sodium channels. Claim 14 encompasses nucleic acids that encode the N-terminal methionine of the encoded protein, followed by a stop codon, and the remainder of SEQ ID NO:1. Clearly such a nucleic acid could not be used as disclosed, as it would encode a totally nonfunctional protein.

The prior art of record (Rudinger, cited in office action mailed 22 August 2006) indicates that it is very difficult to assign function to specific amino acids within protein sequences. Applicant is directed to the office action mailed 22 August 2006, specifically pages 5 – 6, for a more thorough discussion of this matter. Changing the nucleic acid sequence would be expected to lead to mutated non-functional proteins. The specification does not disclose to the skilled artisan how to use those nucleic acids which do not encode sodium channels. Claim 14, part (c) encompasses nucleic acids 95% identical to the complement of SEQ ID NO:1, but the specification does not disclose how to use the full scope of such nucleic acids. As the claim reads on a very large number of possible nucleic acid sequences for which enablement has not been demonstrated, and because the specification fails to provide guidance in determining how to use those nucleic acids which do not encode functional sodium channels, claim 14 clearly reads on an unreasonably large number of possible sequences that could not be used in the absence of a great deal of experimentation. The skilled artisan would essentially have to determine, on his or her own, how to use those nucleic acids which do not encode functional proteins. Given the paucity of guidance and the lack of working examples on point to nucleic acids which do not encode sodium channels, the large degree of experimentation required to make and use the full scope of claim 14 would clearly be undue. In order to expedite prosecution, it is recommended that applicant amend claim 14 part(c) to read "...95% identical to SEQ ID NO:1, wherein the nucleic acid encodes a sodium channel".

Claims 17 and 20 are rejected as they depend from claim 14 but are not limited to enabled embodiments. Claim 24 also is drawn to a large number of possible sequences for which enablement has not been demonstrated and which the skilled artisan could not make in the absence of undue experimentation. The specification fails to disclose to the skilled artisan the full scope of the nucleic acids which are indicative of an increased risk of epilepsy. While a few mutations in SCN1A-encoding nucleic acid are reported at pp. 55 – 57 of the specification, such disclosure is not commensurate in scope the breadth of claim 24. Claim 24 only requires 95% sequence identity to SEQ ID NO:1, as it depends from base claim 14. There is no requirement that any particular region of the nucleic acid be conserved or present. There is no

requirement for mutation at any particular nucleotide. Thus the skilled artisan would have to determine which nucleotide positions within SEQ ID NO:1 are indicative of the subject having an increased risk of epilepsy. Given that SEQ ID NO:1 is over 8000 nucleotides long, a great deal of experimentation would certainly be necessary in order to determine which positions are indicative of increased risk. Wallace (US 7,078,515) teaches that single base pair changes within sodium channel 1A sequences do not result in an increased risk of epilepsy, as some of these polymorphisms are found equally often in control patients and those with epilepsy (Wallace, column 17 lines 52 – 58). Thus the effects of changing nucleic acid sequences in sodium channel genes on risk for epilepsy is unpredictable. Coupled with the relatively small disclosure of positions which in fact confer increased risk of epilepsy to subjects, the large amount of experimentation required to make the full scope of nucleic acids of claim 24 would clearly be undue.

Claim 25 depends from rejected claims and is therefore rejected as well. While certain specific nucleotide positions are recited, claim 25 ultimately depends from claim 14, which is not enabled over its full scope as set forth above. Thus claim 25 encompasses nucleic acids which do not encode proteins and for the reasons set forth above the skilled artisan could not make and use the full scope of the invention of claim 25 in the absence of undue experimentation.

5. Claims 14, 17, 20, and 24 – 25 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The specification fails to describe to the public the full genus of nucleic acid sequences encompassed by claim 14. Claim 14, part (c), encompasses nucleic acids at least 95% identical to SEQ ID NO:1 or to the full-length complement thereof. Claim 14 part(c) does not require that any particular structural element be present in the nucleic acid sequence. The skilled artisan cannot immediately visualize those structures which are common to all members of this genus. A genus claim may be supported by a representative number of species as set forth in *Regents of the University of California v Eli Lilly & Co,* 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), which states:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention". Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1980) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d 1565, 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id at 1170, 25 USPQ2d at 1606."

In the instant case, the specification discloses SEQ ID NO:1 and a few mutants. However the specification fails to describe all nucleic acid sequences at least 95% identical to SEQ ID NO:1. Applicant is directed the Revised Written Description Interim Guidelines Training Materials, available on the internet at <http://www.uspto.gov/web/offices/pac/writtendesc.pdf>, which is analogous to the instant situation. See particularly Example 14, which indicates that claims to biological sequences which also recite relevant function can be considered to be adequately described. Amendment of claim 14 part(c) to read "...95% identical to SEQ ID NO:1, wherein the nucleic acid encodes a sodium channel" may help advance prosecution.

Claims 17 and 20 are rejected as they depend from rejected claim 14 but are not limited to those members of the genus which could reasonably be considered to be fully described. Claim 24 is also not fully described. The specification fails to disclose to the public those structures which are required for the claimed nucleic acids, and fails to set forth the positions within SEQ ID NO:1 which, when altered, lead to "an increased risk of idiopathic generalized epilepsy" as claimed. While certain examples falling within the scope of this genus are described, the full genus has not been described. SEQ ID NO:1 is over 8000 nucleotides long; disclosure of a handful of single nucleotide polymorphisms cannot reasonably be considered to

indicate that applicant was in possession of the full genus of nucleic acids which, when present in a sample of a subject, indicate increased risk of this form of epilepsy.

Claim 25 depends from rejected claims and is therefore rejected as well. While certain specific nucleotide positions are recited, claim 25 ultimately depends from claim 14, which is not fully described as set forth above. Thus claim 25 encompasses nucleic acids which do not meet the written description requirement for the reasons set forth above the skilled artisan could not immediately envision the genus of products encompassed claim 25.

6. Claim 25 stands rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

This rejection stands for the reasons previously made of record and reiterated below. Claim 25 refers to mutations at specific nucleotide positions within SEQ ID NO:1 that the specification as originally filed does not disclose. See office action mailed 30 March 2007, p. 9. Applicant argues that there is implicit support for mutation at nucleotide 828 in the disclosure as originally filed, because the specification discloses a mutation at amino acid residue 188, and that the skilled artisan, cognizant of the genetic would recognize that this corresponds to nucleotide 828. It is not immediately obvious to the examiner how amino acid residue 188 corresponds to nucleotide number 828. Three nucleotides code for a single amino acid. Therefore amino acid position 188 should be encoded by the three nucleotides surrounding position 564, not position 828. In fact, the specification explicitly states that "[b]y sequencing an affected patient and a control, an A-T substitution at nucleotide 565 was found. ... The A565T substitution correspond to a non-conservative amino acid change (D188V)." (specification, p. 55, lines 7 – 15) The specification clearly supports an A-T substitution at nucleotide 565, not 828 as claimed. Therefore, claim 25, part (a), recites new matter.

Applicant argues, on p. 9 of the remarks, that support for mutations at positions 3978 and 5582 of SEQ ID NO:1 can be found in p. 52 and Figure 3. The examiner has closely studied the relevant sections of the disclosure as filed but cannot find support for the invention now claimed. The cited sections disclose mutations at amino acid residues 1238 and 1773. Given that 3 nucleotides encode a single amino acid, this corresponds to nucleotide positions

3714 and 5319 respectively. However claim 25 part (b) is directed to position 3978, not position 3714, and part (c) is directed to position 5581, not 5319. The disclosure as filed fails to support the invention recited in claim 25. Therefore the new matter rejection is maintained.

Priority

7. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120, 121, and 119(e) as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed applications, Application Nos. 09/718355 and 60/167623, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. The examiner is unable to find support for mutations at the specific positions recited in claim 25 as set forth in the new matter rejection above. There is not support in the instant application, and as the instant application is a division of 09/718355 and has the same disclosure, there is not support in the parent application either. After careful review of the provisional application, the examiner is unable to find support for mutations at the positions recited in claim 25. While the provisional application discusses mutations at amino acid residues 1238 and 1773, it does not disclose a mutation at amino acid residue 188. The first time a mutation was disclosed at residue 188 was 24 November 2000, the date 09/718355 was filed. However, since neither 09/718355 nor 60/167623 disclose the invention of claim 25, the effective filing ate of claim 25 is 17 September 2003, the date the instant application was filed.

Conclusion

8. Claims 14, 17, 20, and 24 – 25 are rejected.

9. Claim 23 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The art made of record and not relied upon is considered pertinent to applicant's disclosure. Wallace et al. (U.S. Patent 7,078,515, issued 18 July 2006, PCT filed 20 December 2001). The patent is directed to similar subject matter but has a later effective filing date than all pending claims except claim 25. Furthermore while Wallace discloses nucleic acids encoding human SCN1A channels, those nucleic acids are 8381 bp long (see Wallace, column 16 lines 27 – 39 as well as Wallace's SEQ ID NO:1 and 3), whereas applicant's SEQ ID NO:1 and 2 are 8378 bp long. Additionally Wallace teaches mutations in SCN1A channels at amino acid residues 188, 4057, and 4968, which correspond to nucleic acid positions 563, 1353, 1656 respectively (Wallace, column 17 lines 13 – 51).

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel Kolker whose telephone number is (571) 272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Daniel E. Kolker
Patent Examiner

Daniel E. Kolker, Ph.D.
September 6, 2007